CLAIMS

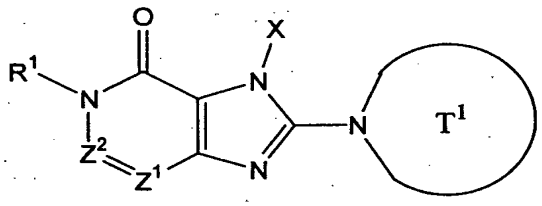
1. A pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and a biguanide agent in combination.

2. The pharmaceutical agent according to claim 1, which enhances the effects of active circulating glucagon-like peptide-1 (GLP-1) and/or active circulating glucagon-like peptide-2 (GLP-2).

3. A pharmaceutical agent that enhances the effects of active circulating GLP-2.

4. A pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and the pharmaceutical agent according to claim 3 in combination.

5. The pharmaceutical agent according to claim 1 or 4, wherein the dipeptidyl peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(I)

(wherein,

T^1 represents a monocyclic or bicyclic 4- to 12-membered heterocyclic group containing one or two nitrogen atoms in the ring, that may have one or more substituents;

X represents a C_{1-6} alkyl group which may have one or more substituents, a C_{2-6} alkenyl group which may have one or more substituents, a C_{2-6} alkynyl group which may have one or more substituents, a C_{6-10} aryl group which may have one or more substituents, a 5 to 10-membered heteroaryl group which may have one or more substituents, a C_{6-10} aryl C_{1-6} alkyl group which may have one or more substituents, or a 5 to 10-membered heteroaryl C_{1-6} alkyl group which may have one or more substituents;

Z^1 and Z^2 each independently represent a nitrogen atom or a group represented by the formula $-CR^2=$;

R^1 and R^2 each independently represent a group according to the formula $-A^0-A^1-A^2$

(A^0 represents a single bond or a C_{1-6} alkylene group, which may have 1 to 3 substituents selected from group B consisting of the substituents described below;

A^1 represents a single bond, an oxygen atom, a sulfur atom, a sulfinyl group, a sulfonyl group, a carbonyl group, a group represented by the formula -O-CO-, a group represented by the formula -CO-O-, a group represented by the formula $-NR^A-$, a group represented by the formula $-CO-NR^A-$, a group represented by the formula $-NR^A-CO-$, a group represented by the formula $-SO_2-NR^A-$, or a group represented by the formula $-NR^A-SO_2-$;

A^2 and R^A each independently represent a hydrogen atom, a halogen atom, a cyano group, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a 5 to 10-membered heteroaryl C_{1-6} alkyl group, a C_{6-10} aryl C_{1-6} alkyl group, or a C_{2-7} alkylcarbonyl group;

however, A^2 and R^A each independently may have 1 to 3 substituents selected from the substituent group B described below:

when Z^2 is a group represented by the formula $-CR^2=$, R^1, and R^2 may in combination form a 5 to 7-membered ring;

except in cases where: [1] R^1 is a hydrogen atom; Z^1 is a nitrogen atom; and Z^2 is –CH=; and [2] Z^1 is a nitrogen atom; and Z^2 is -C(OH)=;

<Substituent group B>

Substituent group B represents the group consisting of: a hydroxyl group, a mercapto group, a cyano group, a nitro group, a halogen atom, a trifluoromethyl group, a C_{1-6} alkyl group which may have one or more substituents, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a group represented by the formula $-SO_2-NR^{B1}-R^{B2}$, a group represented by the formula $-NR^{B1}-CO-R^{B2}$, a group represented by the formula $-NR^{B1}-R^{B2}$ (where R^{B1} and R^{B2} each independently represent a hydrogen atom or a C_{1-6} alkyl group), a group represented by the formula $-CO-R^{B3}$ (where R^{B3} represents a 4 to 8-membered heterocyclic group), a group represented by the formula $-CO-R^{B4}-R^{B5}$ and a group represented by the

formula $-CH_2-CO-R^{B4}-R^{B5}$ (where R^{B4} represents a single bond, an oxygen atom, or a group represented by the formula $-NR^{B6}-$; R^{B5} and R^{B6} each independently represent a hydrogen atom, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic C_{1-6} alkyl group, a C_{6-10} aryl C_{1-6} alkyl group, or a 5 to 10-membered heteroaryl C_{1-6} alkyl group)).

6. The pharmaceutical agent according to claim 5, wherein T^1 is a piperazin-1-yl group or a 3-amino-piperidin-1-yl group.

7. The pharmaceutical agent according to claim 5, wherein T^1 is a piperazin-1-yl group.

8. The pharmaceutical agent according to any one of claims 5 to 7, wherein X is a 3-methyl-2-buten-1-yl group, a 2-butynyl group, a benzyl group, or a 2-chlorophenyl group.

9. The pharmaceutical agent according to any one of claims 5 to 7, wherein X is a 2-butynyl group.

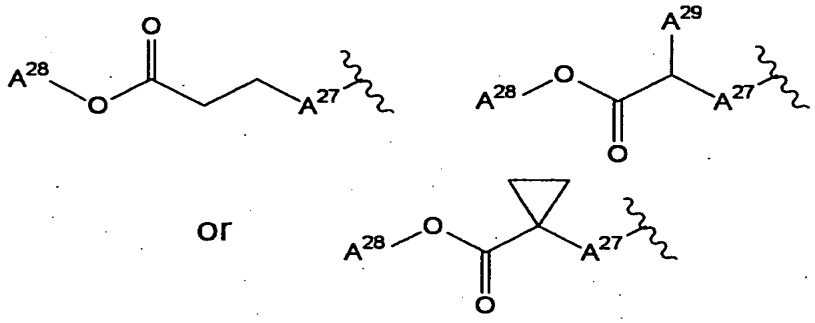
10. The pharmaceutical agent according to any one of claims 5 to 9, wherein,
Z^1 is a nitrogen atom; and
Z^2 is a group represented by the formula $-CR_2=$
(where R^2 is as defined in claim 5).

11. The pharmaceutical agent according to any one of claims 5 to 9, wherein,
Z^2 is a nitrogen atom; and
Z^1 is a group represented by the formula $-CR_2=$
(where R^2 is as defined in claim 5).

12. The pharmaceutical agent according to any one of claims 5 to 11, wherein R^1 is either a methyl group, a cyanobenzyl group, a fluorocyanobenzyl group, a phenethyl group, a 2-methoxyethyl group, or a 4-methoxycarbonylpridin-2-yl group.

13. The pharmaceutical agent according to any one of claims 5 to 11, wherein R^1 is a methyl group, or a 2-cyanobenzyl group.

14. The pharmaceutical agent according to any one of claims 5 to 13, wherein R^2 is either a hydrogen atom, a cyano group, a methoxy group, a carbamoylphenyloxy group, or a group represented by the formula:



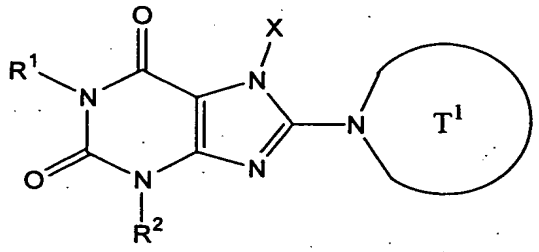
(where,
A^{27} represents an oxygen atom, a sulfur atom, or -NH-;
A^{28} and A^{29} each independently represent a hydrogen atom or a C_{1-6} alkyl group).

15. The pharmaceutical agent according to any one of claims 5 to 13, wherein R^2 is a hydrogen atom, a cyano group, or a 2-carbamoylphenyloxy group.

16. The pharmaceutical agent according to claim 5, wherein the compound represented by formula (I) is any one compound selected from:
(1) 7-(2-butynyl)-2-cyano-1-methyl-8-(piperazin-1-yl)-1,7-dihydropurin-6-one;
(2)
3-(2-butynyl)-5-methyl-2-(piperazin-1-yl)-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;
(3)
2-(3-aminopiperidin-1-yl)-3-(2-butynyl)-5-methyl-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;
(4) 2-[7-(2-butynyl)-1-methyl-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purin-2-yloxy] benzamide;
(5)
7-(2-butynyl)-1-(2-cyanobenzyl)-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purine-2-carbonitrile; and
(6) 2-[3-(2-butynyl)-4-oxo-2-(piperazin-1-yl)-3,4-dihydroimidazo[4,5-d] pyridazin-5-ylmethyl] benzonitrile;
or a salt or hydrate thereof.

17. The pharmaceutical agent according to claim 1 or 4, wherein the dipeptidyl

peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(II)

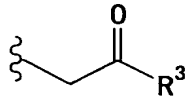
(wherein T^1, X, R^1, and R^2 are as defined in claim 5).

18. The pharmaceutical agent according to claim 17, wherein T^1 is a piperazin-1-yl group.

19. The pharmaceutical agent according to claim 17 or 18, wherein X is a 2-butynyl group or a 2-chlorophenyl group.

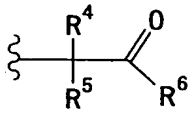
20. The pharmaceutical agent according to claim 17 or 18, wherein X is a 2-butynyl group.

21. The pharmaceutical agent according to any one of claims17 to 20, wherein R^1 is a hydrogen atom, a methyl group, a 2-propynyl group, a 2-butynyl group, a cyanomethyl group, a phenethyl group, a phenoxyethyl group, or a group represented by the formula:



(where R^3 represents a hydroxyl group, a C_{1-6} alkoxy group, or a phenyl group).

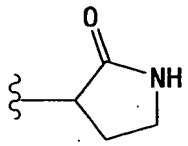
22. The pharmaceutical agent according to any one of claims 17 to 21, wherein R^2 is a hydrogen atom, a C_{1-6} alkyl group, an ethoxyethyl group, a tetrahydrofuranylmethyl group, or a group represented by the formula:



(where,

R^4 and R^5 are identical to or different from each other, and independently represent a hydrogen atom, a methyl group, or a phenyl group; and

R^6 represents a hydroxyl group, a C_{1-6} alkoxy group, or a phenyl group),
or a group represented by the formula:



23. The pharmaceutical agent according to claim 17, wherein the compound represented by formula (II) is any one compound selected from:

(1) 7-(2-butynyl)-1,3-dimethyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(2) 7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(3) methyl
[7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetate;
(4)
7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-1-(2-propynyl)-3,7-dihydropurine-2,6-dione;
(5) 1,7-bis(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(6) [7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetonitrile;
(7)
7-(2-butynyl)-3-methyl-1-[(2-oxo-2-phenyl)ethyl]-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(8) 7-(2-butynyl)-3-ethyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(9) methyl
[7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
(10)
7-(2-butynyl)-3-(2-tetrahydrofuranyl)methyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(11) methyl
[7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]phenylacetate;
(12) 7-(2-butynyl)-3-propyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(13)
7-(2-butynyl)-3-(2-oxo-2-phenethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(14) ethyl
2-[7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] propionate;
(15)
7-(2-butynyl)-3-(2-ethoxyethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(16)
7-(2-butynyl)-3-isopropyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(17)
7-(2-butynyl)-3-(3,3-dimethyl-2-oxobutyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(18)
7-(2-butynyl)-1-methyl-3-(2-oxopyrrolidin-3-yl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(19)
7-(2-butynyl)-3-(2-ethoxyethyl)-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(20) methyl
[7-(2-butynyl)-2,6-dioxo-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
(21) ethyl
[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
(22)
[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
(23)
7-(2-butynyl)-3-[2-oxo-2-(pyrrolidin-1-yl)ethyl]-1-(2-phenethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
(24)
2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-methylacetamide;
(25)
2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-cyclopropyl acetamide;
(26)

2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-phenylacetamide; and

(27)

2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-(2-propynyl) acetamide;

or a salt or hydrate thereof.

24. The pharmaceutical agent according to claim 1, wherein the biguanide agent is metformin.

25. The pharmaceutical agent according to claim 1 or 2, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2.

26. The pharmaceutical agent according to claim 25, wherein the disease is at least any one selected from the group consisting of: diabetes, obesity, hyperlipidemia, and gastrointestinal diseases.

27. The pharmaceutical agent according to claim 3 or 4, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2.

28. The pharmaceutical agent according to claim 27, wherein the disease is a gastrointestinal disease.

29. A method for preventing or treating a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2, which comprises administering the pharmaceutical agent according to claim 1 or 2 at an effective amount.

30. The use of the pharmaceutical agent according to claim 1 or 2 for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2.

31. A method for preventing or treating a disease which is associated with active circulating GLP-2, which comprises administering the pharmaceutical agent according to claim 3 or 4 at an effective amount.

32. The use of the pharmaceutical agent according to claim 3 or 4 for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2.

33. A method for enhancing the effects of active circulating GLP-1 and/or active circulating GLP-2, which comprises using the pharmaceutical agent according to claim 1 or 2.

34. A method for enhancing the effects of active circulating GLP-2, which comprises using the pharmaceutical agent according to claim 3 or 4.